

#15/R.T.  
4/25  
C



DOCKET NO.: ISIS-4797 (ISIC-0002-100)

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

TECH CENTER 1600/2900

APR 25 2003

RECEIVED

In re application of:

Examiner:

Achim H. Krotz

James Shultz

Serial No.: 09/902,953

Group Art Unit: 1635

Filed: July 11, 2001

Confirmation No. 9234

For: **ENHANCEMENT OF THE STABILITY OF OLIGONUCLEOTIDES  
COMPRISING PHOSPHOROTHIOATE LINKAGES BY ADDITION OF WATER-  
SOLUBLE ANTIOXIDANTS**

**BOX RCE**

Assistant Commissioner for Patents  
Washington, D.C. 20231

**Express Mail No.: EV146607497US**

**Date: April 21, 2003**

**AMENDMENT AND REQUEST FOR RECONSIDERATION**

In response to the Office Action mailed November 20, 2002 and Advisory Action mailed March 26, 2003, in connection with the above-identified patent application and Request for Continued Examination filed herewith, Applicant respectfully requests entry of the following amendments and reconsideration in view of the remarks provided below.

**In the Claims:**

Please amend claims 1, 8, and 14 according to the clean version provided below.

C1  
1. (amended twice) A bi-phasic or multiphasic formulation comprising an aptamer, ribozyme, peptide nucleic acid, or antisense oligonucleotide or bioequivalent thereof having one or more phosphorothioate linkages, and a water-soluble anti-oxidant capable of inhibiting desulfurization of said oligonucleotide.